2-Pyrrolidinone, 1-methyl-: Human health tier III assessment

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Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3,000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk

on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted and published separately, using information available at the time, and may be undertaken at different tiers.

This chemical or group of chemicals are being assessed at Tier III because the Tier II assessment indicated that it needed further investigation. The report should be read in conjunction with the Tier II assessment.

For more detail on this program please visit: www.nicnas.gov.au.

Disclaimer

Acronyms & Abbreviations

Synopsis

The chemical N-methyl-2-pyrrolidone (NMP) is a widely used solvent with a variety of applications in cosmetics and domestic products available for consumers. In Australia, the chemical NMP is currently listed in Schedules 5 (25 %) and 6 (50 %) of the Poisons Standard. Based on the international restrictions as well as potential reproductive and developmental toxicity of the chemical, changes to poisons scheduling may be required to manage the potential risks to public health and safety.

Quantitative risk assessments were conducted using a margin of exposure (MOE) approach to evaluate the potential health risks associated with exposure to NMP used in cosmetic and domestic products, as well as from the potential migration of the chemical from wooden toys and other articles.

The chemical is a skin and eye irritant and has effects on body weight, liver, kidney, spleen, and thymus. However, developmental toxicity is considered the most consistent and sensitive effect for human health risk assessment. Therefore, the exposure assessments focused on pregnant women and women of childbearing age. It is assumed that exposures that would not put these women in risk, would also not expose and, therefore, protect other populations including men and children. Public exposure to cosmetics was estimated based on the common use scenarios for products potentially containing the chemical. ConsExpo 4.1 software tool was used to estimate the exposure from domestic products. Publicly available exposure estimates were used to assess the exposure due to migration from articles.

This assessment indicated no unacceptable risk from NMP migration from articles or under the use scenarios evaluated, from the exposures to domestic products containing up to 25 % NMP. On the other hand, presence of NMP in cosmetics at levels above 2 % poses unacceptable risk to users and therefore management of risk for such uses is recommended.

IMAP Human Health Tier II Assessment for NMP can be accessed online and contains detailed assessment information that remains valid (NICNAS). New or updated information is included in the Tier III human health report, in the relevant sections. The Tier II and Tier III reports should be read together.

Rationale for Tier III Assessment

Based on the IMAP Tier II Human Health Hazard assessment, the critical health effects (developmental effects as described in Tier II assessment) have potential to pose an unreasonable risk from the identified uses (public and workers), unless further regulatory controls are applied. Therefore, more detailed human health risk assessment was recommended to determine if public and/or workers are at risk, and if regulatory actions are required to manage the risk(s).

Based on previous mandatory and/or voluntary calls for information, the total volume of NMP introduced into Australia was between 100 and 1000 tonnes, with domestic, commercial and site-limited uses (see details under **Import, Manufacture & Use (Australia)** in the Human Health Tier II Assessment of NMP; NICNAS). Based on products available in Australia or internationally, consumers are expected to be exposed to the chemical through the use of coating (paints, writing inks) and cleaning products (paint strippers, glue and grease removers, sealant removers) that are readily available on the market. In addition, although use in cosmetic products in Australia is not known, the chemical is reportedly used in cosmetic and personal care products overseas at unknown concentrations (SCCS, 2011; CIUCUS, 2011).

In Europe, the use of NMP in consumer products is expected to decline as a result of its entry in Annex VI of the CLP Regulation including Repr. 1B H360D with a specific concentration level (SCL) of 5 % (ECHA RAC, 2014a). Furthermore, in August 2014, The European Chemicals Agency Committee for Risk Assessment (ECHA RAC) assessed the current SCL of 5 % for NMP in light of existing and new information on its reproductive and developmental toxicity (EHCA RAC, 2014b). The Committee adopted an opinion that the current SCL of 5 % should be removed and a general concentration limit of 0.3 % for Category 1 reproductive toxicants should be used instead. If applied, this will effectively restrict the use of NMP in consumer applications to <0.3 % and would, therefore, in effect prohibit the chemical from being used in such products because NMP would have no functionality at this level in present consumer applications (ECHA RAC, 2014b). In addition, in Europe, using carcinogenic, mutagenic, or reproductive toxic (CMR) 1A or 1B substances in cosmetics is prohibited under Article 15(2) of the Cosmetics Regulation 1223/2009. The chemical is, therefore, restricted in cosmetic products irrespective of the concentration limit (EU Regulations, 2009). However, due to the lack of concentration limits in consumer products in other countries, the concentration of NMP in products available for consumers in Australia could be significantly higher.

Extensive literature exists on the toxicity of NMP. A number of adverse effects have been identified in different studies such as skin and eye irritation, effects on body weight, liver, kidney, spleen, thymus, and testicular effects as well as neurotoxicity (NICNAS). The most consistent and sensitive effect considered biologically relevant for human risk assessment is decreased body weight gain observed consistently in oral, dermal and inhalation exposure studies (NICNAS, SCCS, 2011; ECHA RAC, 2014a; US EPA, 2015). Therefore, the reduced foetal body weight is considered a most sensitive and relevant toxic endpoint for determination of human health risks. In addition, the United States Environmental Protection Agency (US EPA) also considered other developmental effects including delayed ossification, skeletal malformations and increased foetal and pup mortality in their risk assessment (US EPA, 2015).

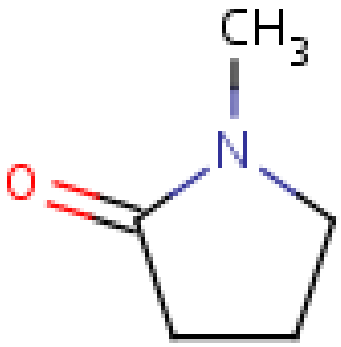
The chemical is currently listed in the Poisons Standard in Schedule 6, with cut-offs to 50 % for Schedule 5 listing and 25 % as exempt, consistent with it being listed as a designated solvent (SUSMP, 2016). Based on the available data and international reports on cosmetic (SCCS, 2011) and domestic (ECHA, 2013) uses, NICNAS (NICNAS) recommended that the potential risks to public health and safety be managed through changes to the Poisons Scheduling. To further validate the recommendation, the relevance of observed health effects for human health will be discussed and quantitative risk assessment for the use of cosmetics and domestic products containing NMP is conducted using a MOE approach. In addition, as NMP is also commonly used in surface treatment of various articles including wooden toys, the potential migration of the NMP from articles will be evaluated.

The Tier II assessment recommended that SafeWork Australia consider the adequacy of current controls concerning inhalation exposure, and that further risk assessment may be required. To date, this recommendation remains subject to consultations being undertaken by SafeWork Australia and will not be further progressed at this point.

The purpose and scope of this Tier III assessment is to determine the human health risks from NMP used in consumer products such as cosmetics, cleaning and coating products as well as from possible migration from articles such as wooden toys, particularly from repeated or prolonged exposure.

Chemical Identity

Synonyms	N-methyl-2-pyrrolidone

	N-methyl pyrrolidone 1-methylazacyclopentan-2-one methyl pyrrolidone NMP
Structural Formula	
Molecular Formula	C5H9NO
Molecular Weight (g/mol)	99.13
Appearance and Odour (where available)	A clear liquid with a mild amine odour.
SMILES	C1(=O)CCCN1C

Import, Manufacture and Use

Australian

In addition to the information provided in the Tier II assessment, use of the chemical is identified in hair dye stain removal products (cosmetic and personal care use) as identified based on online searches of products containing NMP, and in spot removal products (domestic use reported under previous mandatory and/or voluntary calls for information).

International

The specific uses identified for NMP are based on online searches of products containing NMP as well as the following publications and databases: ECHA, 2011; ECHA, 2013; Danish EPA, 2015; US EPA, 2015; Chemical/Product Categories Database (CPCat); and United States Household Products Database (US HPD).

The chemical has been reported as being used in a limited number (<30) of cosmetic products in the US (CIUCUS, 2011). The final concentration of NMP in cosmetic products is not known (SCCS, 2011).

In addition to the information provided in Tier II assessment, use of the chemical is identified in following cosmetic and personal care products:

- hair dye products (semi-permanent)
- hair dye stain removal products
- hair styling products
- facial creams
- foot callus peeling cream
- shower products
- mascaras
- eyeliners
- artificial nail removers
- nail polish removers

Use of the chemical is identified in following non-cosmetic products that may be available for general public (domestic and do-it-yourself (DIY)):

- inks (artists colours, inkjet inks, pen inks)
- grease, sealant, glue and paint removal products
- paints and other coatings (e.g. floor varnishes)
- cleaning products (e.g. spot stain remover)

Restrictions

Australian

This chemical is listed in the Poisons Standard (the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP)) in Schedules 5 and 6.

- Schedule 6 except (a) when included in Schedule 5; or (b) in preparations containing 25 % or less of designated solvents.

Schedule 6 chemicals are labelled with 'Poison'. These are substances with a moderate potential for causing harm, the extent of which can be reduced by using distinctive packaging with strong warnings and safety directions on the label.

- Schedule 5 (a) when packed in single use containers having a capacity of 2 mL or less; or (b) in preparations containing 50 % or less of N-methyl-2-pyrrolidone or preparations containing 50 % or less of a mixture of any two or more of N-methyl-2-pyrrolidone, N-(N-octyl)-2-pyrrolidone or N-(Ndodecyl)-2-pyrrolidone **except** in preparations containing 25 % or less of designated solvents.

Schedule 5 chemicals are labelled with 'Caution'. These are substances with a low potential for causing harm, the extent of which can be reduced through the use of appropriate packaging with simple warnings and safety directions on the label.

A list of designated solvents is provided in the SUSMP.

International

European Union

Using CMR 1A or 1B substances in cosmetics is prohibited under Article 15(2) of the Cosmetics Regulation 1223/2009. Therefore the chemical is restricted in cosmetic products, irrespective of the concentration limit (EU Regulations, 2009).

The chemical is listed on the candidate list of substances of very high concern (SVHC) for Authorisation (ECHA, 2011).

The chemical has and entry in Annex VI of the Classification, Labelling and packaging (CLP) Regulation including Repr. 1B H360D with a SCL of 5 %. In August 2014, the ECHA RAC (2014b) agreed that the current SCL of 5 % for the developmental effects (Repr. 1B H360D) should be removed and the general concentration limit (GCL) of 0.3 % for Repr 1B chemicals should be applied. If applied, this will effectively restrict the use of NMP in consumer applications to <0.3 % and thereby would be an effective ban on such products because NMP would have no functionality at this level in present consumer applications.

Existing Work Health and Safety Controls

Hazard Classification

The chemical is classified as hazardous with the following risk phrases for human health in the Hazardous Substances Information System (HSIS) (Safe Work Australia):

- R61 Repr. Cat. 2 (developmental toxicity)
- Xi; R36/37/38 (irritation)

The R61 classification currently has a specific concentration limit of >5 %.

Exposure Standards

Australian

The chemical has an exposure standard of 103 mg/m^3 (25 ppm) time weighted average (TWA) and 309 mg/m^3 (75 ppm) short-term exposure limit (STEL). The exposure standard includes a notation that absorption through the skin may be a significant source of exposure (Safe Work Australia).

International

The following exposure standards are identified (Galleria Chemica):

- An exposure limit (TWA) of 4–400 mg/m^3 (1–100 ppm) in different countries such as USA (Alaska, Hawaii), Canada (Yukon), Norway and Switzerland.
- In the opinion of ECHA RAC, those conducting a REACH chemical safety assessment should be obliged to use long term ‘derived no effect levels (DNEL)’ of 10 mg/m^3 (2.5 ppm) for inhalation exposure and 4.8 mg/kg/day for dermal exposure for workers as the basis for their risk characterisation (ECHA RAC, 2014c). The joint ECHA RAC and the Scientific Committee on Occupational Exposure Limits (SCOEL) opinion is expected to be adopted in February 2016.

- In Germany, the German Ad-hoc Group on Indoor Guidelines of the Indoor Air Hygiene Committee and the States' Supreme health Authorities have also issued indoor air guide values for the chemical. Based on their assessment, the Guide value II (RW II – Health hazard value) was set as 1 mg/m^3 (0.25 ppm) and the Guide value I (RW I – precautionary value) as 0.1 mg/m^3 (0.025 ppm) (Bundesgesundheitsbl, 2014). These guide values are calculated based on continuous exposure (6–24 hours; 5–7 days).

Exposure

Public Exposure

Public exposure to NMP is estimated for scenarios including its use in cosmetics and personal care products as well as in domestic products including coatings and cleaning products. In addition, the potential migration from articles treated with products containing NMP is evaluated.

NICNAS and several international organisations (ECHA RAC, 2014c; US EPA, 2015) have identified developmental and reproductive toxicity as the critical health effects of NMP, and therefore, pregnant women are likely to be the most sensitive population. However, any decisions protective for pregnant women are also expected to protect other populations including men and children. In this assessment, the reasonable worst-case approach is used, in which estimates are based on worst-case, but plausible, exposure scenarios. It is believed that this approach will address practically all individuals within the target population.

Exposure from cosmetic and personal care products

Sources of exposure

The chemical is used as a solvent in cosmetic and personal care formulations. While the full scope of the use of this chemical in Australian is not known, the chemical is known to be present in many types of cosmetic products sold in Australia. The cosmetic and personal care products containing the chemical, as identified internationally, include nail polish removers, artificial nail remover, hair dye stain remover, hair dyes, hair care products, face moisturisers, foot callus creams, shower products, as well as make-up products including mascaras and eye liners. Concentrations of NMP in cosmetic and personal care products are not known (SCCS, 2011). The European Union (EU) has a current specific concentration limit (SCL) of 5 % NMP in the consumer products. In addition, in Europe, using CMR 1A or 1B substances in cosmetics is prohibited and the chemical is therefore restricted in cosmetic products irrespective of the concentration limit (EU Regulations, 2009). In Australia there are currently no restrictions on concentration limits for NMP in cosmetic products.

As the final concentration of the chemical in cosmetic products is not known (SCCS, 2011), total exposure from consumer products was estimated using nominal concentrations of 10 %, 5 % (current consumer product limit in Europe), 2 %, and 0.3 % (proposed consumer product limit in Europe; ECHA RAC, 2014).

Routes of exposure

The main route of public exposure to NMP from cosmetic and personal care products is through dermal contact. In addition, inhalation exposure may occur while using nail polish, artificial nail removal or hair dye stain removal products (RIVM, 2006). The potential for public exposure from cosmetics and personal care products via oral route is expected to be negligible and hence is not characterised further.

Estimates of dermal exposure

Depending on the type of product, dermal contact with cosmetics and personal care products can be limited to specific areas of the body such as the eye region, face, hands, nails, or feet, or it can be more extensive, covering large areas of the trunk as well as the face. The duration of exposure for various products may differ substantially; for rinse-off products such as soaps or

shampoos, exposure might only be for a few minutes, although some residual product can remain, whereas for leave-on products, exposure could last for several hours.

Dermal exposure to the chemical was calculated as an internal dose which is proportional to the use volumes, product retention factors (reflecting proportions of product remaining on the skin during normal use) and dermal bioavailability of NMP. Dermal bioavailability was assessed based on dermal absorption of the chemical. NMP has been reported to readily permeate the skin, although several factors may affect the dermal absorption such as the vehicle (matrix), occlusion, and the duration of contact. The absorption ranged significantly under various exposure conditions from 7 to 98 % (ECHA RAC, 2014a). Using human skin the highest absorption rate observed was 80 %. Based on the dermal absorption studies a conservative dermal absorption percentage of 100 % was used.

No data on Australian use patterns (for example, typical amount used each application, frequency of use and exposure duration) were available for cosmetics or personal care products. However, data collected on typical use patterns of some classes of these products in Europe are available in the Technical guidance document on risk assessment (TGD) of the European Chemicals Bureau (ECB, 2003) and the Scientific Committee on Consumer Safety's (SCCS) Notes of guidance for the testing of cosmetic substances and their safety evaluation (SCCS 2012). In addition, ConsExpo 4.1 modelling based values were used for certain products (RIVM, 2006). For the purposes of this assessment, Australian use patterns for these products are considered similar to those in Europe and, consequently, data from these overseas sources have been used in determining Australian NMP exposures.

As the reproductive and developmental toxicity was considered to be the most sensitive endpoints for NMP, the adult female body weight of 70 kg was used for the exposure assessment (enHealth, 2012).

The internal dose arising from dermal exposure to cosmetic and personal care products were estimated using Equation 1.

Equation 1

$$D_{int,derm} = \frac{A_{prod} \times n \times \frac{C}{100} \times \frac{B_{derm}}{100} \times RF \times CF}{BW}$$

Where:

$D_{int,derm}$ = Internal dose via the dermal route, µg/kg bw/d
A_{prod} = Amount of cosmetic/personal care product applied to skin, mg/event
n = Frequency of product application, event/d
C = Concentration of NMP in product, % (w/w)
B_{derm} = Bioavailability via the dermal route, %
RF = Retention factor
CF = Conversion factor, 1000 µg/mg
BW = Adult female bodyweight, 70 kg

The exposure parameters used for calculation of internal NMP doses from dermal exposure ($D_{int,derm}$) from different product types are shown in Table 1.

Table 1: Exposure parameters used for calculation of internal dose from dermal exposure ($D_{int,derm}$) from cosmetic and personal care products.

Product type	**A_{prod} – (mg product)**	**n (event/day)**	**RF**
Leave-on products			
Hair dye stain remover	8500 [a]	0.05 [b]	1

Product type	A_{prod} – (mg product)	n (event/day)	RF
Nail polish remover	200 $	0.43 $	1
Artificial nail remover	200 c	0.14 d	1
Mascara	25 #, $	1 #, $	1
Eyeliner	5 #, $	1 #, $	1
Hair styling products	4000 &	1.14 &	1
Face moisturiser	800 #	2 #	1
Rinse-off products			
Hair dye (semi-permanent)	30000 #	0.05 #	0.1
Shower products	5000 #	2 #	0.1
Foot callus cream	1200 e	0.07 e	0.1

= ECB, 2003: Technical Guidance Document on Risk Assessment.

$ = RIVM, 2006: Cosmetics Fact Sheet.

& = SCCS, 2012: The SCCS's notes of guidance for the testing of cosmetic substances and their safety evaluation. 8th Revision.

a = Estimated based on amount of nail polish remover used per nail area (500 mg/15 cm^2; RIVM, 2006). It is assumed that the exposed area will be total of 269 cm^2. This is based on ¼ hands (fingers; 0.25×840 cm^2 = 210 cm^2; ECB, 2003) and 1/20 head surface (0.05×1180 cm^2 = 59 cm^2; ECHA, 2008). The area exposed is therefore 17-fold of that of fingernails and the total amount of products will be 17×500 mg = 8500 mg.

b = Based on frequency of applications of semi-permanent hair dyes (ECB, 2003).

c = Based on the amount of nail polish remover (above).

d = Frequency estimated as once a week.

e = Amount based on default foot antiperspirant cream (RIVM, 2006).

f = Frequency based on suggested use of cream twice a month.

For the worst-case scenario estimation under these assumptions, if a person were a simultaneous user of all the products listed in Table 1, the combined internal dose from NMP dermal exposure ($D_{int,derm}$) is determined to be 0.294, 1.956, 4.890 and 9.781 mg/kg bw/day for products containing NMP at 0.3, 2, 5, and 10 %, respectively (refer to Table 3).

Estimates of inhalation exposure

Inhalation exposure to the chemicals in cosmetic and personal care products commonly occur through use of spray products. Inhalation exposure is also expected after use of nail products. Similarly, inhalation exposure is expected to occur during use of hair dye stain removal products as the composition and the use of the product is assumed similar to nail polish removal products.

For the estimation of the internal dose from the use of these products, the following parameters/assumptions were used:

- an adult inhalation rate is 20 m^3/day (95th percentile; enHealth 2012);
- a conservative estimate of NMP bioavailability through inhalation of 100 % will be used (ECHA RAC, 2014a);
- the average body weight in women is 70 kg (enHealth, 2012);
- the exposure duration estimate is 5 min (RIVM, 2006); and
- a room volume of 2 m^3 to represent the volume of air immediately surrounding the user (EC 2003), except for nail products where the application of nail polish products is assumed to occur close to face and therefore volume of 1 m^3 is used (RIVM, 2006).

The internal dose arising from inhalation exposure to cosmetic and personal care products were estimated using Equation 2.

Equation 2

$$D_{int,inh} = \frac{A_{prod} \times n \times \frac{C}{100} \times \frac{B_{inh}}{100} \times t \times IR_{air} \times CF_1 \times CF_2}{BW \times V_{room}}$$

Where:

$D_{int,inh}$ = Internal dose via the inhalation route, µg/kg bw/day
A_{prod} = Amount of cosmetic/personal care product applied on skin or nail, mg/event
n = Frequency of spray application, event/day
C = Concentration of NMP in product, %
B_{inh} = Bioavailability via the inhalation route, %
t = Time of contact (spray and exposure duration), minute
IR_{air} = Inhalation rate of person, m^3/d
CF_1 = Conversion factor (time), 1 d/1440 minutes
CF = Conversion factor (amount), 1000 µg/mg
V = Room volume, m^3
BW = Adult female body weight, kg.

The frequency and amount of products used as well as calculations of NMP internal inhalation doses ($D_{int,inh}$) are shown in Table 2.

For the worst-case scenario estimation under these assumptions, if a person were a simultaneous user of all the products listed in Table 2, the combined internal dose from NMP inhalation exposure ($D_{int,inh}$) is determined to be 0.015, 0.102, 0.255 and 0.509 mg/kg bw/day for products containing NMP at 0.3, 2, 5, and 10 %, respectively (refer to Table 3).

Table 2: Exposure parameters and calculated daily internal dose from inhalation exposure ($D_{int,inh}$) to cosmetic and personal care products.

Product type	mg product/event	n (event/day)	Vroom (m^3)
Nail polish remover	500 $	0.43 $	1
Artificial nail remover	500 b	0.14 c	1
Hair dye stain remover	8500 d	0.03 d	2

= ECB, 2003: Technical Guidance Document on Risk Assessment.

$ = RIVM, 2006: Cosmetics Fact Sheet.

& = SCCS, 2012: The SCCS's notes of guidance for the testing of cosmetic substances and their safety evaluation. 8th Revision.

a = Note that the total amount applied per nail is greater than the amount of product touching the dermal boundary of the nail (Table 1; RIVM, 2006).

b **=** Amount based on nail polish remover (above).

c = Frequency estimated as once a week.

d = See above for dermal exposure.

Combined exposure from contact with cosmetic and personal care products

The estimated systemic exposure to NMP, and internal dose (D_{int}) arising from the combined use of cosmetic and personal care products at the assumed maximum levels, is summarised in Table 3. Exposure via dermal route is estimated to be the major route of NMP exposure from cosmetic products with the inhalation exposure contributing to only about 5 % of the total exposure (refer to Table 3).

Table 3: Total estimated exposure to NMP from cosmetic and personal care uses at different concentrations of the chemical in the products as well as percentage of total exposure via different routes.

Route of exposure	Dint (mg/kg bw/day)				Percentage of total exposure
	0.3 %	2 %	5 %	10 %	
Dermal	0.294	1.956	4.890	9.781	95
Inhalation	0.015	0.102	0.255	0.509	5

Combined	**0.309**	**2.058**	**5.145**	**10.290**	**100**

Uncertainties in exposure assessment from cosmetic and personal care products

In comparison to the present assessment, the European Commission Scientific Committee on Consumer Safety (SCCS), in its safety evaluation of NMP in cosmetic products, used a conservative exposure of 17.8 g product/day (SCCS, 2011). When 5 % NMP concentration in products and 70 kg body weight are assumed, an internal exposure of 12.7 mg/kg bw/day is obtained. This is significantly higher than the estimated internal dose in the present assessment. The exposure estimate used by SCCS is a global daily exposure volume for all cosmetic products that one person may daily apply on the skin and therefore a worst case scenario (currently 17.4 g/day; SCCS, 2012). In the present assessment, the exposure was estimated based on the volume of known cosmetic products containing NMP, and is therefore less conservative.

As the NOAEC was derived for inhalation exposure of NMP, the average air concentration of NMP from us of the cosmetic and personal care products containing NMP could have been estimated. However, the expected inhalation exposure from cosmetic and personal care products containing NMP was expected to be a minor contribution to overall exposure, and therefore the internal dose, instead of concentration was used for the exposure assessment. The exposure assessment confirmed the assumption of low contribution of inhalation exposure, as it was estimated to be only 5 % of total exposure.

While outside to the scope of the present assessment, NMP can also be used in pharmaceuticals as a solvent or penetration enhancer for a transfer of substances through the skin. It has been suggested that NMP may be one of the main pharmaceutical co-solvents (Jouyban et al., 2010). Therefore, the presence in pharmaceutical products may increase the exposure of certain individuals.

Exposure from domestic products

Sources of exposure

The chemical NMP is used as a solvent in various coatings including paints, varnishes and inks as well as in cleaning products including spot stain removers, paint removers, glue and grease removers and sealant removers. For example, products sold in Australia contain up to 60 % or more NMP in paint removal products and up to 30 % in stain removal products.

Currently, the chemical is included in Schedule 5 at 25 % and in Schedule 6 at 50 % (SUSMP). Therefore, total exposure from consumer products will be estimated using various set concentrations of 50, 25, 5 % (current consumer product limit in Europe) and 0.3 % (adopted consumer product limit in Europe; ECHA RAC, 2014b).

Dermal and inhalation exposure to the chemical was estimated as an internal dose using the ConsExpo4.1 (RIVM, 2006). No data on Australian use patterns (for example, typical amount used each application, frequency of use and exposure duration) were available for domestic products. Therefore, default values for typical use patterns of these products during an event were derived from ConsExpo model 4.1 (Bremmer and van Engelen, 2007; Burg et al., 2007). For the purposes of this assessment, Australian use patterns for these products are considered similar and, consequently, default data from ConsExpo model 4.1 have been used in determining Australian NMP exposures (see further details below). For determination of inhalation exposure, the ConsExpo also allows the model to limit the air concentration to the vapour pressure of pure substances. This will limit the calculated maximal air concentration corresponding to the saturated air concentration of the pure compound.

Routes of exposure

The main route of public exposure to NMP from domestic products is expected to be through inhalation, but dermal exposure is also possible during application and removal of the coating and cleaning products. The potential for public exposure via oral route is expected to be negligible and, hence, is not characterised further.

Estimates of dermal exposure

Dermal contact with coating and cleaning products can be limited to specific areas of the body, mainly on hands if gloves are not used. As the NMP is used as a solvent in these products, evaporation of the NMP is expected to occur over relatively short time frame and the maximum exposure is expected from the initial contact with hands. However, dermal absorption of NMP is expected to be fast (ECHA, 2011).

In ConsExpo, the dermal exposure was modelled based on following parameters (refer to Table 4 for further details):

- the average body weight in women (70 kg; enHealth, 2012)
- dermal bioavailability (B_{derm}; 100%; ECHA RAC, 2014a)
- total amount of product (A_{prod}, mg; variable)
- area of skin exposed (A_{skin}, cm^2; variable)
- events per year (n; variable)

In addition, when modelling the dermal exposure from application of paints by brushing and rolling as well as application of glue removers, a parameter called the 'contact rate' (Rate, mg/min) is used together with the exposure time (T, min). This describes the rate at which the coating is applied to the skin (mg/min) (Bremmer and van Engelen, 2007; Burg et al., 2007).

The exposure parameters used for calculation of internal NMP doses from dermal exposure ($D_{int,derm}$) to different product types are shown in Table 4. In this assessment, the reasonable worst-case scenario is used and therefore, the exposure is modelled based on overhead painting of normal viscosity product (e.g. solvent rich paint) expected to contain the highest percentage of NMP and thereby resulting in greater exposure (Bremmer and van Engelen, 2007).

Table 4: Exposure parameters used for calculation of internal dose from dermal exposure ($D_{int,derm}$) from domestic products (Bremmer and van Engelen, 2007; Prud'homme de Lodder et al., 2006; Burg et al., 2007).

Product type	A_{prod} (mg product)	Rate (mg/min)	n (event/ year)	A_{skin} (cm^2)	T (min)
Coatings					
Paints (overhead brush – normal viscosity)	- [a]	60	2	-	120
Floor lacquer	250	-	0.33	108 [b]	-
Writing inks	10	-	365	1[c]	-

Product type	A_{prod} (mg product)	Rate (mg/min)	n (event/ year)	A_{skin} (cm^2)	T (min)
Cleaning					
Spot stain remover[d]	70	-	10	230[e]	-
Paint remover	500	-	1	430[f]	-
Glue/Grease remover	-	30	0.25	-	240
Sealant/foam remover	100	-	5	5[g]	-

a = Only parameters used for the calculation of internal dose using ConsExpo 4.1 are included in the table

b = Estimated area of both hands (Burg et al, 2007)

c = Estimated 1 cm^2 of the skin will be covered in ink (Burg et al, 2007)

d = Estimated for carpet spot stain remover (Prud'homme de Lodder et al., 2006)

e = Corresponds to the area of fingers of both hands (Burg et al, 2007)

f = Corresponds to the area of palms of both hands (Burg et al, 2007)

g = Corresponds to area of fingers of one hand (Burg et al, 2007)

For the worst-case scenario estimation under these assumptions, if a person were a simultaneous user of all the products listed in Table 1, the combined internal dose from dermal exposure ($D_{int,derm}$) is determined to be 0.002, 0.038, 0.190, 0.379 mg/kg bw/day for products containing at 0.3, 5, 25 and 50 % NMP, respectively.

Estimates of inhalation exposure

Inhalation is the main route of exposure from the use of domestic products. As a worst case scenario, it is assumed that 100 % of the substance is in the consumer product will be released at once into the room (ECHA, 2012).

In ConsExpo, the dermal exposure is modelled based on following parameters (refer to Table 5 for further details):

- the average body weight in women (70 kg; enHealth, 2012)
- adult female inhalation rate during medium activity (36 m^3/day for medium activity; enHealth, 2012)

- bioavailability via inhalation route (B_{inh}; 100%; ECHA RAC, 2014a)
- room volume (V_{room}, m^3; variable)
- total amount of product (A_{prod}, g; variable)
- ventilation rate (V_{rate}, h-1; variable)
- number of events per year (n; variable)

The exposure parameters used for calculation of internal NMP doses from inhalation exposure ($D_{int,inh}$) from different product types are shown in Table 5. In this assessment, the reasonable worst-case scenario is used and therefore, the exposure is modelled based on use of solvent rich paints, expected to contain the highest concentration of NMP as a solvent (Bremmer and van Engelen, 2007). As found in the human risk assessment for paint strippers or graffiti removing products containing NMP by the United States Environmental Protection Agency, Office of Pollution Prevention and Toxics (EPA/OPPT) in 2015 (US EPA, 2015), the NMP concentration in the air was limited by the maximal air concentration corresponding to the saturated air concentration (C_{Sat}) of the pure compound. C_{Sat} was based on temperature (20°C), vapour pressure of NMP at 20°C (32 Pa) and molecular weight of NMP (99.13 g/mol) (DFG, 1998). C_{Sat} of NMP is achieved at approximately 1300 mg/m^3.

Table 5: Exposure parameters used for calculation of internal dose from inhalation exposure ($D_{int,inh}$) to cosmetic and personal care products (Bremmer and van Engelen, 2007; Prud'homme de Lodder et al., 2006; Burg et al., 2007; enHealth, 2012).

Product type	**A_{prod} (g product)**	**n (event/year)**	**T (min)**	**V_{room} (m^3)**	**V_{rate} (h^{-1})**
Coatings					
Paints (solvent rich paints)	1000	2	132	20	0.6
Floor varnish/lacquer	3000	0.33	60	15	1.5
Writing inks	-[a]	-	-	-	-
Cleaning					
Spot stain remover	-[a]	-	-	-	-

Product type	A_{prod} (g product)	n (event/year)	T (min)	V_{room} (m^3)	V_{rate} (h^{-1})
Paint remover	1000	1	60	20	0.6
Glue/Grease remover	2000	0.25	240	30	1.5
Sealant/foam remover	100	5	180	10	2

a = Inhalation exposure from the use of writing inks and spot stain removers is considered negligible due to small volumes of use (ECHA, 2011).

Based on the C_{Sat} and inhalation exposure parameters shown in Table 5, the maximum individual product mean concentrations on day of exposure ranged 54.3-217 mg/m^3 for products containing 50 and 25 % of NMP, 10.4-113 mg/m^3 for 5 % NMP and 0.623-12.9 for mg/m^3 for 0.3 % NMP. For the maximum event concentrations, the C_{Sat} was reached during the use of most products containing 25 or 50 % of NMP.

The combined worst-case scenario cumulative daily average inhalation air concentrations (C_{inh}) for NMP were determined to be 0.079, 1.022, 1.712 and 2.411 mg/m^3 for products containing NMP at 0.3, 5, 25 and 50 %, respectively.

Uncertainties in exposure assessment from domestic products

The use of personal protective clothing, particularly gloves was determined to be effective in reducing the exposure estimates in the risk assessment for the paint and graffiti removers by the United States Environmental Protection Agency (US EPA, 2015). However, the use of protective clothing was not assumed in this risk assessment as consumers will not necessarily use protective clothing even when use is recommended by the manufacturer (ECHA, 2012). Therefore, as the exposure estimate was based on reasonable worst-case scenario, no protective clothing was assumed in exposure assessment.

Exposure via migration from articles

NMP may be present in articles due to its presence in various surface treatment products or as a residual in plastics (EFSA, 2005). While the NMP is assumed to mainly evaporate following application, it has been detected for example in surface treated wooden toys (Danish EPA, 2005). NMP is expected to be contained within the articles, and could migrate, for example to food from food contact non-stick surfaces like cooking pans, baking trays and microwave containers or from mouthing of toys by children.

NMP can be present in relevant articles including:

- wooden surfaces including wooden toys (Danish EPA, 2005), due to its use as a solvent in various lacquers, varnishes and paints;
- coatings to provide non-stick qualities, including bakeware and cooking pots and pans; and
- high temperature thermoplastics e.g. in microwave oven safe containers (EFSA, 2005).

Exposure from wooden toys

Danish Environmental Protection Agency (Danish EPA) analysed the migration of the chemical NMP from surface-treated wooden toys and evaluated the potential oral exposure of children less than three years old due to mouthing of the toys (Danish EPA, 2005). The parameters used to calculate the uptake of NMP by oral exposure were:

- oral absorption of 100 %
- exposure time of 3 hours
- body weight of 10 kg (child)
- total migration ranging 29-62 µg/10 cm^2/hour (Danish EPA, 2005)

The estimated oral uptake varied between 9-19 µg/kg bw/day.

Exposure from migration to food

European Food Safety Authority evaluated substances intended for use in materials in contact with food (EFSA, 2005). They concluded that no detectable migration of NMP from polymers used in microwave safe containers was found under the test conditions (EFSA, 2005). Based on this analysis, NMP is not expected to migrate from articles to food. However, if information becomes available on such migration, the exposure via this route should be reanalysed.

Health Hazard Information

Key studies for hazard assessment

The studies used to derive the no-observed-adverse-effect-level (NOAEL) and the no-observed-adverse-effect-concentration (NOAEC) for developmental effects are briefly described below. Further details of these studies can be found in the Human Health Tier II assessment of NMP. As the main routes of exposure are dermal and inhalation, the NOAEL and NOAEC obtained from inhalation and dermal developmental toxicity studies were considered most relevant. However, the oral toxicity studies were also considered as supporting evidence for the dermal and inhalation studies. Little first-pass metabolism is indicated based on almost identical metabolism identified for NMP administered by dermal and oral routes (WHO, 2001; Danish EPA, 2015).

Dermal study

In two dermal developmental toxicity studies in rats, a dermal NOAEL ($NOAEL_{derm}$) of 237 mg/kg bw/day was established based on reduced numbers of pups, reduced foetal body weight and indications of retarded skeletal development at the next higher dose of 750 mg/kg bw/day (ECHA, 2013). Maternal toxicity, indicated by reduced body weight gain, was reported at 750 mg/kg bw/day. However, the effects observed in offspring were considered chemical-related rather than a consequence of maternal toxicity (ECHA RAC, 2014c; see discussion below).

The $NOAEL_{derm}$ of 237 mg/kg bw/day is supported by another dermal developmental toxicity study in Himalayan rabbits, with the NOAEL for maternal and developmental toxicity was reported as 1000 and 300 mg/kg bw/day, respectively.

Inhalation study

In a 6 hour/day inhalation study in rats (see IMAP Human Health Tier II assessment for details) an inhalation NOAEC ($NOAEC_{inh}$) of 0.247 mg/L was established based on statistically significant decreases in foetal body weight at the next higher dose (0.494 mg/L). A dose-dependent but slight decrease in foetal body weights was also detected at lower doses. Reduced body weight was also observed in dams, but the reduction was not significant when corrected for the weight of the gravid uterus. The reduced pup body weights observed in this study were also observed in a two-generation rat inhalation study (Solomon et

al., 1995; ECHA RAC, 2014c) where the reduced foetal body weight at 0.478 mg/L persisted until weaning, supporting adversity of the effect.

Oral studies

In two multigenerational toxicity studies performed according to OECD TG 416, the observed oral NOAEL ($NOAEL_{oral}$) for developmental (pup mortality and reduced body weight gain) and maternal toxicity in Sprague-Dawley (SD) and Wistar rats was 160 mg/kg bw/day (see IMAP Human Health Tier II assessment for details; NICNAS).

In another oral developmental toxicity study in rats (see IMAP Human Health Tier II assessment for details; NICNAS) an $NOEAL_{oral}$ of 125 mg/kg bw/day was established based on reduced foetal body weights. Maternal toxicity occurred at the 500 mg/kg bw/day dose as shown by reduced maternal body weight.This $NOAEL_{oral}$ is also supported by another developmental toxicity study in rats (Exxon, 1992). Reduced foetal body weight and increased incidence of stunted foetuses were reported at 400 mg/kg bw/day, with no significant toxicity observed at lower dose of 125 mg/kg bw/day. The maternal body weight gain was reduced at 400 mg/kg bw/day, but the reduction was not significant when corrected for gravid uterine weight. In addition, no changes were observed in food consumption.

In a developmental toxicity study in New Zealand White rabbits, offspring mortality and malformations were increased at 540 mg/kg bw/day while no significant developmental toxicity was reported at lower dose of 175 mg/kg bw/day. Dose-dependent reductions in maternal body weight gain and food consumption were reported at 540 mg/kg bw/day. Reduced maternal body weight gain was also reported at 175 mg/kg bw/day but only between gestation days 6-12 and food intake was not affected at this dose. No maternal toxicity was reported at lowest dose of 55 mg/kg bw/day. The $NOAEL_{oral}$ for developmental and maternal toxicity in this study were 175 and 55 mg/kg bw/day, respectively.

In a recent reproductive and developmental toxicity study, not discussed in the Tier II assessment, female Wistar rats were administered 0, 150, 450 and 1000 mg/kg bw/day NMP by gavage, 5 days/week for about 9 weeks (2 weeks before mating and 1 week of mating, 3 weeks of gestation, and 3 weeks of lactation) (Sitarek et al., 2012). Statistically significant maternal toxic effects including reduced body weight during gestation were observed at all doses. A reduced number of live pups was observed in the high dose group. Fertility index was reduced at two highest doses and the percentage of pups that survived was significantly reduced in the 150 and 450 mg/kg bw/day groups. Reduced bodyweight was observed in offspring at day 4 (150 and 450 mg/kg bw/day exposure groups), 7, 14, 21 (all 450 mg/kg bw/day exposure group). The oral lowest-observed-adverse-effect-level ($LOAEL_{oral}$) for developmental toxicity was set at 150 mg/kg bw/day (developmental effects reported are not considered secondary to maternal toxicity; see discussion below), which is the lowest LOAEL found in the developmental studies on NMP. An $NOAEL_{oral}$ could not be established as the effects were seen at all doses.

Therefore, based on the lowest reported $LOAEL_{oral}$ of 150 mg/kg bw/day, the oral $NOAEL_{oral}$ of 125 mg/kg bw/day was chosen as a highest oral $NOAEL_{oral}$ below the reported $LOAEL_{oral}$ for the risk assessment.

Relevance of observed health effects

Reduced body weight is the most sensitive and consistent effect observed following NMP exposure (males, females and pups). This effect is also detected in dams following maternal exposure, and notably, the pregnant females appear to be more sensitive than the general animals (Danish EPA, 2015). Therefore, the contribution of maternal toxicity to developmental effects is difficult to determine. However, reduced foetal weight was observed at the lower dose than the maternal toxicity in the key oral developmental toxicity study used to derive the NOAEL for risk assessment (see Key studies for hazard assessment). In addition, in a two-generation rat inhalation study (Solomon et al, 1995) and another oral developmental toxicity study (Exxon, 1992), decreased pup body weights were detected without effects on the maternal body weight. These studies indicate that the effects on the pups are direct rather than a secondary unspecific effect of maternal toxicity. While in other developmental toxicity studies (NICNAS), a decrease in body weight gain was detected in pregnant dams, it was considered that the reduced maternal body weight gain was not sufficient to explain the decreased pup body weights, and therefore, the pup effect is not likely to be a secondary effect on maternal toxicity (ECHA RAC, 2014a; US EPA, 2015).

As there is no data to indicate rodent-specific mechanisms, it is assumed that the reduced body weight observed in the animal studies is relevant for humans. Therefore, an effect on foetal growth is expected to be the most sensitive endpoint in humans. It is not possible to translate the decreased birth weight observed in the animal studies into an expected outcome in humans.

However, it can be concluded that the decreased birth weight in general may be a disadvantage for the later development of the baby and/or adult health of the individual concerned (ECHA RAC 2014a).

Selection of the NOAEL for Risk Assessment

The main exposure to cosmetics is expected to be via dermal route (refer to Table 3), and for the domestic products via the inhalation route (refer to Table 6). Therefore, the $NOAEC_{inh}$ of 0.247 mg/L and $NOAEL_{derm}$ of 237 mg/kg bw/day derived from dermal and inhalation studies, respectively, were chosen for the risk assessment.

Supporting the dermal and inhalation studies, the lowest $LOAEL_{oral}$ reported for developmental toxicity following oral exposure was 150 mg/kg bw/day (Sitarek et al., 2012). Therefore, the most relevant $NOAEL_{oral}$ for oral exposure was considered to be 125 mg/kg bw/day, which was the highest NOAEL closest to the lowest $LOAEL_{oral}$. This developmental toxicity $NOAEL_{oral}$ was also supported by multiple other studies including the two generation studies in rats ($NOEAL_{oral}$ of 160 mg/kg bw/day; NICNAS; SCCS, 2011), developmental toxicity study in New Zealand White rabbits ($NOEAL_{oral}$ of 175 mg/kg bw/day; NICNAS).

Risk Characterisation

Public Risk Characterisation

Methodology

A margin-of-exposure (MOE) methodology is commonly used to characterise risks to human health associated with exposure to chemicals (ECB, 2003). The risk characterisation is conducted by comparing quantitative exposure information with a NOAEL/NOAEC selected from appropriate animal studies and deriving an MOE as follows:

1. Identification of critical health effect(s).
2. Identification of the most appropriate/reliable NOAEL for the critical health effect(s).
3. Comparison of the estimated or measured human dose or exposure (EHD) with the appropriate/reliable NOAEL to provide an MOE:
MOE = NOAEL/EHD.
4. Evaluation whether the MOE obtained by this method indicates a health concern for the human population under consideration.

The MOE provides a measure of the likelihood that a particular adverse health effect will occur under the conditions of exposure. As the MOE increases, the risk of potential adverse effects decreases. To decide whether the MOE is of sufficient magnitude, expert judgement is required. Such judgements are usually made on a case-by-case basis, and should take into account uncertainties arising in the risk assessment process such as the completeness and quality of the database, the nature and severity of effect(s) and intra/inter species variability. With the interspecies and intraspecies assessment factors of 10, the acceptable MOE for NOAEL-based assessment is 100.

In this assessment, the MOE methodology was used for characterising the public health risks from NMP exposure through use of cosmetic and personal care products as well as through use of domestic products by the general population.

Risk estimates

Risk estimate related to use of cosmetics and personal care products

The main route of exposure to NMP from cosmetic use in the general population is through dermal contact (95 %). Inhalation exposure is also possible from certain products, but is assumed to be minimal (5 %). Oral exposure is considered negligible as current information does not indicate NMP use in products, such as toothpastes, mouthwashes, lipsticks and lip-glosses that are prone to accidental oral ingestion.

A the main exposure to NMP from the cosmetic and personal care product use was estimated to be via dermal route, the dermal $NOAEL_{derm}$ of 237 mg/kg bw/day was chosen for the calculation of MOE. The combined, worst-case scenario internal dose from NMP dermal and inhalation exposure (D_{int}) is determined to be 0.309, 2.058, 5.145 and 10.29 mg/kg bw/day for products containing NMP at 0.3, 1 and 5 %, respectively (refer to Table 3). Based on these values, the MOEs given in Table 6 were calculated.

Table 6: Calculated MOE for the critical health effect of NMP from estimated aggregate exposure to cosmetic products for the general population

Concentration of NMP (%)	$NOAEL_{derm}$ (mg/kg bw/day)	D_{int} (mg/kg bw/day)	MOE
10	237	10.290	23
5	237	5.145	46
2	237	2.058	115
0.3	237	0.309	768

The estimated MOE for developmental toxicity in the general population is less than 100 (refer to Table 6) at NMP concentrations of 5 % in cosmetic and personal care products, while the MOE is close to 100 for the NMP concentrations of 2 %. This indicates a risk of developmental toxicity in the general population from use of multiple cosmetic products containing NMP at 2 % or higher. Therefore, risk management is required.

Risk estimate related to use of domestic products

The main routes of exposure to NMP from use of domestic products in the general population are the inhalation and dermal routes. Oral exposure is considered negligible. Therefore, the risk assessment for domestic products was performed separately for dermal exposure and for inhalation exposure.

Dermal $NOAEL_{derm}$ of 237 mg/kg bw/day for developmental toxicity was used for assessment of risk arising from dermal exposure to domestic products containing NMP. The worst-case scenario internal NMP doses from dermal ($D_{int.derm}$) exposure were determined to be 0.002, 0.038, 0.190 and 0.379 mg/kg bw/day for products containing NMP at 0.3, 5, 25 and 50 %, respectively. Based on these values, the MOEs for dermal (MOE_{derm}) exposure were calculated (refer to Table 7).

Table 7: Calculated MOEs for the critical health effect of NMP from estimated dermal exposure from domestic products for the general population.

Concentration of NMP (%)	$NOAEL_{derm}$ (mg/kg bw/day)	$D_{int.derm}$ (mg/kg bw/day)	MOE_{derm}
50	237	0.379	625

Concentration of NMP (%)	$NOAEL_{derm}$ (mg/kg bw/day)	$D_{int.derm}$ (mg/kg bw/day)	MOE_{derm}
25	237	0.190	1250
5	237	0.038	6248
0.3	237	0.002	104128

The $NOAEC_{inh}$ of 0.247 mg/L (247 mg/m^3) was used for the assessment of risk arising from inhalation exposure to domestic products containing NMP. The worst-case scenario average daily NMP concentrations (C_{inh}) exposures were determined to be 0.079, 1.022, 1.712 and 2.411 mg/m^3/day for products containing NMP at 0.3, 5, 25 and 50 %, respectively. Based on these values, the MOEs for inhalation (MOE_{inh}) exposure were calculated (refer to Table 8).

Table 8: Calculated MOEs for the critical health effect of NMP from estimated inhalation exposure from domestic products for the general population.

Concentration of NMP (%)	$NOAEC_{inh}$ (mg/kg bw/day)	C_{inh} (mg/m^3/day)	MOE_{inh}
50	247	3.450	102
25	247	1.722	144
5	247	1.022	242
0.3	247	0.079	3138

Total MOE (MOE_{tot}) was developed for exposures from the combined routes were based on following equation: $MOE_{tot} = 1/(1/MOE_{derm} + 1/MOE_{inh})$. Calculate MOE_{tot} for the critical health effect of NMP from estimated dermal and inhalation exposure from domestic products for the general population is shown in Table 9.

Table 9: Calculated total MOEs for the critical health effect of NMP from estimated dermal and inhalation exposure from domestic products for the general population.

Concentration of NMP (%)	MOE_{derm}	MOE_{inh}	MOE_{tot}
50	625	102	**88**
25	1250	144	**129**
5	6248	242	**233**
0.3	104128	3138	**3046**

Based on the estimated total MOEs for developmental toxicity following dermal or inhalation exposure from domestic products in the general population, the MOE is greater than 100 (refer to Table 9) up to the NMP concentration of 25 % in domestic products. This indicates that the risk of developmental toxicity in the general population from the use of domestic products containing 25 % or less NMP is low.

This assessment did not consider public risk from the possibility of the chemical to be present in air fresheners (Basement Health Association). If use in such products at significant concentrations is confirmed, the public risk to consumer products including air fresheners should be reanalysed.

Risk estimate related to migration from wooden toys

Based on the Danish EPA analysis (Danish EPA, 2005) the estimated oral uptake in children was estimated to be between 9-19 µg/kg bw/day (0.009-0.019 mg/kg bw/day). As the exposure is via the oral route, the $NOAEL_{oral}$ derived from oral toxicity studies were used for the risk assessment. While the $NOAEL_{oral}$ selected for the present risk assessment is based on the reproductive toxicity, it is assumed to be protective for all populations including children. Therefore, $NOAEL_{oral}$ of 125 mg/kg bw/day was used to estimate the possible health risk in children arising from mouthing of wooden toys. The lowest MOE was >6500 (125/0.019=6579). Therefore, no unacceptable health risk is detected.

NICNAS Recommendation

Further risk management is required. Based on the quantitative risk assessment, public exposure to cosmetic products containing 2 % or more of the chemical NMP may lead to unacceptable health risk due to reproductive toxicity of the chemical. Therefore, it is recommended that risks to public health and safety from the potential use of the chemical in cosmetic and personal care products should be managed through changes to poison scheduling. It is recommended that cosmetic products containing NMP should be placed in Schedule 6 except where the NMP concentration is less than or equal to 2 %.

Advice for consumers

Products containing the chemical should be used according to instructions on the label

Advice for industry

The advice provided in the human health Tier II IMAP report remains unchanged.

A review of the physical hazards of the chemical has not been undertaken as part of this assessment.

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